PN-ABZ-309
91904

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1. Project/Subproject Number: 931-1018

2. Contract/Grant Number: DPE-5984-Z-00-9018-00

3. Publication Date: 1993

4. Document Title/Translated Title:
Malaria Chemoprophylaxis Compliance in Pregnant Women: A Cost-Effectiveness Analysis of Alternative Interventions

5. Author(s)
1. Deborah L. Helitzer-Allen
2. Deborah A. McFarland
3. Jack J. Wirima
4. Allen P. Macheso

6. Contributing Organization(s)
Academy for Educational Development (HEALTHCOM project)

7. Pagination: 5

8. Report Number:

9. Sponsoring A.I.D. Office: Bureau for R&D/Office of Health

10. Abstract (optional - 250 word limit)

11. Subject Keywords (optional)
1.
2.
3.
4.
5.
6.

12. Supplementary Notes
published in Social Science and Medicine 36, no. 4, 1993, 403-407

13. Submitting Official: Willard Shaw

14. Telephone Number: 202-884-8789

15. Today's Date: 4-17-95

DO NOT write below this line

16. DOCID:

17. Document Disposition
DOCRD [] INV [] DUPLICATE []

AID 590-7 (10/88)

Soc. Sci. Med. Vol. 36, No. 4, pp. 403–407, 1993
Printed in Great Britain.

0277-9536/93 $6.00 + 0.00

MALARIA CHEMOPROPHYLAXIS COMPLIANCE IN PREGNANT WOMEN: A COST-EFFECTIVENESS ANALYSIS OF ALTERNATIVE INTERVENTIONS

DEBORAH L. HELITZER-ALLEN,[1] DEBORAH A. MCFARLAND,[2,3] JACK J. WIRIMA[4] and ALLEN P. MACHESO[5]

[1]School of Hygiene and Public Health, Johns Hopkins University, 615 N. Wolfe St, Baltimore, MD 21205, U.S.A., [2]School of Public Health, Emory University, 1599 Clifton Road, Atlanta, GA 30329, U.S.A., [3]International Health Program Office, Center for Disease Control, Atlanta, GA 30333, U.S.A., University of Malawi, College of Medicine, Lilongwe, Malawi, and [5]Ministry of Health, Malawi

Abstract—Compliance to malaria chemoprophylaxis among pregnant women in Malawi has historically been low. Three separate interventions, based upon an ethnographic study of malaria beliefs among pregnant women in Malawi, were introduced to increase compliance to the malaria chemoprophylaxis program provided by the Ministry of Health. Each intervention consisted of a health education message and an antimalarial drug. A cost-effectiveness analysis of the interventions was conducted to compare the interventions as alternative strategies to increase compliance among pregnant women.

Key words—malaria, cost-effectiveness, compliance, health education

1. INTRODUCTION

Malaria during pregnancy is associated with anemia and other complications of pregnancy, including the increased likelihood of delivering a low birth weight infant [1–6]. In Malawi, a country where malaria is endemic, the Ministry of Health (MOH) supports a program of malaria chemoprophylaxis for pregnant women. At each monthly visit a 4 week supply of chloroquine phosphate (300 mg base) is given free of charge to women attending the antenatal clinic to take at home between monthly visits. Health education regarding malaria is also routinely given at the clinic as one of several topics covered during antenatal sessions.

The underlying issue of concern for the MOH is that malaria during pregnancy can be prevented *only* if compliance to the program is high. The problem of low compliance and its effect on health care has been well documented in the literature [7]. Noncompliance is of concern because of its detrimental effects on the quality of medical care through unsuccessful therapies such as antimalarial chemoprophylaxis and on overall quality of life where noncompliance accounts for a considerable portion of illness experienced by the population. For malaria, a preventable illness, noncompliance to regimens during pregnancy lead to high costs for the program and to maternal/infant care in general. Additional research in Malawi has shown that if compliance with the antimalarial chemoprophylaxis program were 80%, the cost of preventing one *P. falciparum* infection among Malawi women would decrease from U.S. $10.87 (at 36% compliance) to U.S. $1.09 [8].

Evaluations conducted routinely by the Malawi MOH malaria research team show that compliance with the current weekly regimen is approx. 25% nationwide [9]. The MOH is interested in low cost interventions which can increase compliance to malaria chemoprophylaxis among women attending the antenatal clinics. Thus a study was undertaken in collaboration with the MOH which had three objectives: (1) to identify obstacles that hinder compliance; (2) to test several alternative interventions to overcome the obstacles identified; and (3) to determine the cost-effectiveness of the alternative interventions. The results of the first two study objectives have been reported previously [10]. We report the results of the cost-effectiveness analysis in this article.

Cost-effectiveness analysis is an economic evaluation technique increasingly used in developing countries for comparing costs and outcomes of alternative interventions to achieve program objectives [11, 12]. However, the cost-effectiveness of health education interventions is rarely reported [13]. For countries like Malawi, struggling to maximize the use of limited resources [14], the results of a cost-effectiveness analysis can provide practical guidance for making decisions regarding resource allocation.

2. METHODS

A. Interventions

Three interventions for increasing compliance were tested in four antenatal clinics in Malawi. The interventions were designed to overcome obstacles identified in the formative research phase of the study. Both the obstacles that hinder compliance and the details of the interventions tested have been reported elsewhere [10]. Briefly, the obstacles identified were

the bitter taste of chloroquine phosphate and a health education message which did not differentiate among several words used to describe malaria in the local language, some of them perceived to be more serious than others. To overcome the bitter taste of chloroquine phosphate, a non-bitter tasting chloroquine preparation was distributed. To address the confusion caused by the health education message used in the current antenatal malaria chemoprophylaxis program, a new health education message was developed which incorporated the findings of the formative research. In essence, the new health education message acknowledged the local belief that the symptoms of headache, fever and chills associated with malaria had several different etiologies. The messages stressed that when the symptoms came from an illness caused by mosquitoes, they were especially dangerous for pregnant women. In addition, the message stressed that the drug chloroquine could prevent the symptoms-when taken correctly.

There were three interventions tested in the four clinic populations (one intervention was tested in two clinics): (1) distribution of chloroquine phosphate and a new health education message (CQ + NHE); (2) distribution of non-bitter tasting coated chloroquine phosphate and the original health education message (CCQ + OHE); and (3) distribution of non-bitter tasting coated chloroquine phosphate and a new health education message (CCQ + NHE). The three interventions were compared to the current malaria chemoprophylaxis program—distribution of chloroquine phosphate and the original health education message (CQ + OHE).

The intervention study was conducted in four clinics in Lilongwe District. Each of the clinics was more than 10 kilometers outside city limits and 20 kilometers from one another. Each was on a tarred road leading to the city and bus service was available.

The four clinic populations were not statistically different in parity or gravidity. There were statistically significant differences in tribal distribution ($\chi^2 = 64.38$, $P = <0.0001$) and education ($\chi^2 = 7.82$, $P = 0.0497$) between the clinics. However, the relationship between use of the medication at enrollment and education, use of the medication at enrollment and tribe, and tribe and education was not significant. Complaints about side effects were significantly different between clinics ($\chi^2 = 76.05$, $P < 0.0001$), but complaints about side effects were not independent of medication use and side effects do not deter women from taking the medication. Finally, during the course of the study, the rates of return to each clinic were approximately the same.

The interventions were tested during the end of the rainy season (April–June) when malaria transmission is highest. Although malaria is endemic in Malawi, the incidence of malaria and malaria-related visits to health centers appears to increase during these months. Epidemiologically, the risk of malaria is higher when the mosquito population has peaked and is declining, because the fewer mosquitoes that are present are older and more likely to be carrying sporozites.

B. Compliance

Urine specimens were collected from women attending the antenatal clinic for the first visit and on their next return visit [8]. Compliance was measured by the presence of one part per million (ppm) of chloroquine phosphate which was considered compatible with the ingestion of a weekly prophylactic dose (300 mg) during the preceding 7 days [15].

Compliance with the current malaria chemoprophylaxis program (CQ + OHE), as reported by the MOH malaria research team and confirmed by baseline measurements in this study, is 25%. In the clinic using the first intervention (CQ + NHE), the return visit (post-intervention) level of compliance was 57%. The return visit level of compliance in the second intervention clinic (CCQ + OHE) was 87% and in the third intervention clinics (CCQ + NHE), the average return visit compliance level was 91% [10].

C. Effectiveness

Effectiveness in this study was defined as the level of compliance with the antenatal malaria chemoprophylaxis regimen achieved by each of the three interventions and by the current antenatal malaria chemoprophylaxis program. Given the short-term programmatic purposes of this analysis, a process measure of effectiveness (level of compliance) was used rather than an outcome measure such as malaria cases or deaths prevented.

D. Cost

Since the three interventions did not require additional health system costs or a change in health services delivery, only incremental costs (additional costs not incurred under the current antenatal malaria program) were estimated in this analysis. The relevant incremental cost categories were drugs, modified health education materials, and training in health communication techniques.

Total drug costs to the MOH were estimated for each intervention for all pregnant women in Malawi in 1988. Applying the most recent data (1986) on the timing of first visits to the antenatal program, by trimester of pregnancy, to the entire 1988 cohort of pregnant women, gave the number of women by trimester in 1988 to receive antenatal malaria chemoprophylaxis. From these numbers, the maximum number of chloroquine phosphate doses for use in the antenatal chemoprophylaxis program was calculated. The assumption was made that women would enroll at the beginning of each trimester and thus receive the maximum number of doses for that trimester (36 doses for those enrolled during the first trimester, 24 for those enrolling in the second trimester, and 12 for those enrolling in the third trimester). Cost in 1988 of uncoated and coated chloroquine phosphate

Table 1. The cost-effectiveness (cost per compliant woman) of alternative interventions to increase use of antimalarial chemoprophylaxis among pregnant women, Malawi, 1988

Intervention		Cost	Compliance levels	Number of compliant women	Cost compliant woman
CQ + OHE (current program)	Drugs	$149,844.45	25%	89,965	$1.67
CQ + NHE	Drugs	$149,844.45	57%	205,119	$1.27
	H Ed	110,000.00			
		$259,844.45			
CCQ + OHE	Drugs	$374,611.14	87%	313,076	$1.20
CCQ + NHE	Drugs	$374,611.14	91%	327,470	$1.48
	H Ed	110,000.00			
		$484,611.14			

was U.S. $9.86/1000 tablets and U.S. $46.00/1000 tablets respectively or U.S. $0.02 and U.S. $0.05 per dose [16].* Multiplying the maximum number of doses times the cost per dose gave the total drug costs for each intervention for the 1988 cohort of pregnant women.

Total incremental costs for new health education materials and training were based on the estimated costs of designing, producing and distributing a flip chart to assist health workers in their health education efforts (U.S. $10.00 per chart) and the cost of refresher training for health workers in new health communication techniques (U.S. $100.00 per clinic) [17]. There are approx. 1000 clinics or health centers in Malawi.

3. ANALYSIS

The estimated number of pregnancies in Malawi for 1988 was 359,857. Of the women registered in antenatal clinics in 1986, 11.8% were in their first trimester of pregnancy at the time of their first visit, 50.3% were in their second trimester of pregnancy, and 37.8% were in their third trimester of pregnancy [18]. Thus 42,463 (11.8%) would require a maximum of 36 doses of antimalarial chemoprophylaxis, 181,008 (50.3%) women would require a maximum of 24 doses, and 134,946 (37.5%) women would require a maximum of 12 doses. A maximum of 7,492,223 doses of antimalarial chemoprophylaxis would have been needed in 1988.

At U.S. $0.02 per dose, the cost of supplying the population of pregnant women in Malawi in 1988 with uncoated chloroquine phosphate would have been $149,844.45; at U.S. $0.05 per dose, the cost of providing coated chloroquine phosphate would have been $374,611.14. The total cost estimate for the health education component was U.S. $110,000 for the 1000 clinics and health centers in Malawi.

*Coated chloroquine phosphate is not available commercially in Malawi. Sterling Products International produces a coated chloroquine phosphate preparation in 500 mg (300 mg base) tablets that is sweet in taste and pink in color. Sterling provided the coated chloroquine phosphate for the intervention study.

Compliance levels shown in Table 1 are those achieved under the current antenatal chemoprophylaxis program and the return visit levels of compliance achieved under the three interventions described above. Applying the post-intervention percentages to the number of pregnant women in Malawi in 1988 gives the maximum number of compliant women in the antenatal malaria chemoprophylaxis program for each intervention. Dividing the cost of the intervention by the maximum number of compliant women gives the cost per compliant woman, a measure of the cost-effectiveness of each intervention.

Table 1 shows the results of the analysis. For the current antenatal malaria chemoprophylaxis program in Malawi (CQ + OHE), the cost per compliant woman is $1.67. When a new health education message is substituted for the original message but the medication is not changed (CQ + NHE), the cost per compliant woman decreases to $1.27. If a coated chloroquine phosphate product is used alone with the original health education message (CCQ + OHE) the cost per compliant woman is $1.20. The combined strategy of a change in medication to a coated chloroquine phosphate preparation and a new health education message (CCQ + NHE) gives a cost per compliant woman of $1.48.

4. DISCUSSION

The cost-effectiveness analysis demonstrates that the three interventions analyzed are each more cost-effective than the current malaria chemoprophylaxis program if the measure of effectiveness is compliance with the chemoprophylaxis regimen. Although an initial hypothesis was that the best strategy to increase compliance would be the combined use of a different product and a new health education message, the results suggest that this would not be the case. Either a strategy of a different medication or a new health education message would be more cost effective than the combined strategy.

The addition of a new medication appears to be the most cost-effective method of enhancing program effectiveness, i.e. increasing compliance. Changing the medication to a coated product would raise the pharmaceutical costs of the program by more than

100% from current levels, but would raise the compliance levels from 25% to 87%. Adding a new health education message to the coated product would increase the cost per user over that of the medication alone. This suggests that the two interventions together may be redundant. However, the combined intervention would still be more cost-effective than the current program.

The use of uncoated chloroquine phosphate supplemented by a new health education message was ranked second among the cost-effectiveness interventions assessed. If implemented this intervention would decrease the cost per woman by 24% from the current program.

The choice for the MOH appears to be between two interventions, uncoated chloroquine phosphate and a new health education message or a non-bitter tasting coated chloroquine phosphate medication, which have similar values of cost-effectiveness when compared to the current antenatal malarial chemoprophylaxis program. If the first intervention (CQ + NHE) is chosen the question becomes whether or not the new health education message can be maintained at the level at which it was tested. Health education messages in the clinics of Malawi would need considerable revision in order to ensure that the topic of malaria and the need for chemoprophylaxis was covered at each clinic session. At present, malaria is one of several health education topics; only one topic is covered at each antenatal session. As with other health education messages, there is likely to be listener burn-out. The challenge is to raise compliance and maintain it at a level high enough to enable the message frequency to be reduced.

The second intervention (CCQ + OHE) did increase compliance to higher levels than uncoated chloroquine phosphate and a new health education message, but the intervention, if implemented nationwide, would require a significantly higher malaria drug investment by the MOH than the current malaria drug investment. The use of a coated chloroquine phosphate product yielded the highest average percentage change in compliance among all the interventions, suggesting that the use of an improved drug may reduce the need for constant reminders through health education messages. This is certainly a strategy to consider if the MOH has additional resources available for drugs.

Results of the cost-effectiveness analysis illustrate the trade-offs faced by the MOH. It can achieve higher compliance levels than the current program by introducing a new health education message but these improvements in compliance may not be sustainable. However, the choice of a new medication, while increasing compliance to even higher levels, increases total drug costs which may be unacceptable in a period when decreased resources are available to the health sector, particularly since drugs most often must be purchased with scarce foreign exchange. Such trade-offs are the reality for those making resource allocation decisions. Use of cost-effectiveness analysis should be used alongside other program and epidemiological data to make responsible decisions. Cost-effectiveness analysis is not a formula for decision-making but should be regarded as an important addition to the decision-maker's analytical tool-kit.

Acknowledgements—The activities reported in this article were supported by the Ministry of Health, Malawi, the Communication for Child Survival, or HEALTHCOM Project, funded by the United States Agency for International Development (USAID), Bureau for Science and Technology, Office of Health and Office of Education (Contact no. DPE-1018-C-00-5063-00) and the Africa Child Survival Initiative, Combatting Childhood Communicable Diseases (Project 698-0421) funded by USAID. HEALTHCOM is conducted by the Academy for Educational Development, Washington, DC. The opinions expressed in this article are those of the authors and not necessarily those of the supporting organizations.

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